which is more than 80% identical to the sequence selected from the sequences in the group consisting of SEQ ID NO. 2 and SEQ ID NO. 4.

REMARKS

Claims 1-6 and 13-23 remain presented for examination. The specification has been amended to add a description for Figure 13. Support for the description of Figure 13 is found in the specification as filed at page 7, in the first full paragraph, page 17 last paragraph, and page 18, third paragraph. Claims 1-5 have been amended as set forth above and new Claims 18-23 have been added. Typographical errors have been corrected in Claims 1, 3, and 5. Support for the amendments and the new Claims is found throughout the application as filed, including the Claims. No new matter has been added by the amendments or by the new Claims.

The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment. On this set of pages, the **insertions are double underlined and bolded** while the **[deletions are in brackets and bolded].**

Discussion of Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-2, and Claims 3-6 which depend from Claim 1, were rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Office Action recitation of the phrase "biological activity" renders the claims vague and indefinite.

Claims 1 and 2 have been amended as set forth above to recite "enzymatic activity" in place of "biological activity." Furthermore, the preamble of Claim 1 has been amended to further define a process that occurs using a processive lipid glycosyl transferase that successively transfers hexose residues to a lipid acceptor.

In view of the amendments to Claims 1 and 2, Applicants assert that the Claims are clear and definite, and respectfully request withdrawal of the instant rejection under § 112, second paragraph.

Discussion of Rejection under 35 U.S.C. § 112, first paragraph

Enablement:

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph as not being enabled. The Office Action asserts that the specification, while being enabling for the process of producing a number of specified exemplary glycolipids, does not reasonably provide enablement for a process of producing any or all types of glycolipids. Also, the Office Action asserts that Claims 1-6, while being enabled for enzymes with the sequence of SEQ ID NOs: 2 or 4, with processive glycosyl transferase (PDG) activity, isolated from *B.subtilis* or *S.aureus*, are not enabled for PDG from any and all sources.

"To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993).

Respectfully, Applicants disagree with the instant rejection of Claims 1-6 and Applicants assert that the Claims are enabled. Applicants assert that the specification teaches those of skill in the art how to make and use the full scope of the claimed invention without undue experimentation. The Examiner is of the opinion that the claims are so broad as to encompass the process of making any glycolipid. However, this is not a correct understanding of the claimed invention.

Claim 1 as amended is enabled because the Claim now further defines the process for the production of glycolipids in transgenic cells and/or organisms as one using a processive lipid glycosyl transferase that successively transfers hexose residues to a lipid acceptor. Furthermore, the claimed process of producing glycolipids is defined by the nucleic acid molecule that is transferred and expressed in transgenic cells and/or organisms. In other words, by defining the claimed process in terms of the processive enzymatic activity of the used lipid glycosyl transferase that is able to successively transfer hexose residues to a lipid acceptor, the claims are enabled by the specification.

The Examiner also asserts that Claims 1-6 while enabling for enzymes with SEQ ID NO:2 or 4, with processive diacylglycerol glycosyltransferase (PDG) activity, isolated from either *B. subtilis* or *S. aureus*, are not enabled for any PDG enzyme from any or all sources.

It should be understood that the processive activity of the enzymes according to the invention is a novel feature that before the priority date of the present application has never been described in the prior art in connection with enzymes of the lipid biosynthesis pathway. This application for the first time described and characterized that a glycosyl transferase involved in lipid biosynthesis binds two different substrates, *i.e.*, a pure lipid in the first step and a lipid-bound sugar in the second and further steps. This means that the principle of the processive glycosylation could be demonstrated in the present invention for the first time, and the proof of principle is provided by describing the enzymes from *S. aureus* and *B. subtilis*. These two examples, in view of the pioneering nature of the invention, provide enablement for the full genus of such enzymes. Thus, even though the application describes two exemplary enzymes, the scope of the claims and enablement is justified in view of the fact that Applicants have discovered the instant pioneering invention.

Furthermore, the skilled artisan following the disclosed teachings and routine methodology can easily make and use any PDG enzyme from any or all sources. The disclosed sequences can be utilized to isolate such sequences from other organisms by the routine techniques described in the specification. Also, as set forth more fully below, the specification provides ample teaching regarding modified enzymes consistent with the full scope of the claimed invention. Specifically for example, the specification at page 6, line 23 to page 7 line 6 teaches how to make PDGs. Therefore, Applicants respectfully request withdrawal of the instant rejection.

Written Description:

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner alleges that the claims are directed to the use of

polypeptides derived from SEQ ID NOs. 2 and 4, while the specification fails to provide description of modified polypeptides encompassed by the claims.

Applicants respectfully disagree and assert that the specification provides ample teaching to describe the full scope of the Claims. To satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991).

The specification describes the claimed invention, including the use of all species of the claimed genus of polypeptides. For example, the specification at page 6 line 23 to page 7, line 6 provides guidance sufficient to describe the full scope of the claimed invention, including teaching for numerous variations in the polypeptide sequences. For example, the proteins can have more than 5 amino acids within the amino acid sequence EHQPDIII. That sequence is identical with the amino acid sequence of the proteins from *B. subtilis* and/or *S. aureus*. Also, the proteins can preferably have more than 6 amino acids within the amino acid sequence QVVVVCGKN or the amino acid sequence DCMITKPG, both of which are identical with the amino acid sequence of the proteins from *B. subtilis* and/or *S. aureus*. Furthermore, for example, more preferably, the encoded protein can include the amino acid sequence MITKPGGITxTE, or the amino acid sequence VKxTGIPI, or the amino acid sequence ZPDIIIxxxP, which are identical to the sequence found in *B. subtilis* and/or *S. aureus*, *and* where x is any amino acid and where Z represents Q or K.

Thus, Applicants have fully described the claimed invention, including the polypeptides, in sufficient detail to demonstrate possession of the full genus of such peptides in compliance with the first paragraph of § 112.

Discussion of Rejection Under 35 U.S.C. § 103

The Examiner rejected Claims 1-3 under 35 U.S.C. § 103(a) as being unpatentable over Sorokin et al. ("Sorokin") (SwissProt Database, Accession No. P54166, October 1996), Kunst et al. ("Kunst") (PIR Database, Accession No C69935, December 1997), and Price et al. ("Price") (J. Bacteriol., 1997, Vol. 179(15):4959-4961.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Respectfully, none of the cited references make the claimed invention obvious, because none alone or in combination provide a process for production of glycolipids, particularly using a protein with processive enzymatic activity. Furthermore, there is no motivation or suggestion to combine the references absent improper hindsight reconstruction of the claimed process.

The identification of the processive enzymatic activity is by no means obvious in view of the cited art. Although galacto lipids can be found in plants that comprise several sugar units, these galacto lipids are not synthesized in the plants by the activity of a processive enzyme, but by the activity of several glycosyl transferases that act independently of each other. One example of those non-processive enzymes is the MGDG synthase, described in Price, which art is cited by the Examiner at page 11 of the office action. The enzyme described in Price is a non-processive galactosyl transferase, which catalyzes the first step. Further galactosylation steps are catalyzed by a second enzyme, which has been described by Kelly and Dormann, *J. Biol. Chem.* (2002) 11, 277.

It is not sufficient to simply use known sequences of the references which code for non-processive enzymes. Rather, the inventors of the present invention had to carry out intensive enzyme assays, as described in the specification, in order to find out and prove that it is just one enzyme that catalyzes more than one glycosylation step in a successive manner, *i.e.*, to demonstrate that the enzyme acts in a processive way.

Further, the MurG enzyme described in the art, is no processive lipid glycosyl transferase according to the present invention. In contrast to the Examiner's opinion, it is not obvious to the skilled person in view of the cited prior art, that the amino acid sequence as described in Sorokin and Kunst is that of a protein with processive glycosyl transferase activity, capable of transferring sugar molecules to lipid substrates. It can even be taken from the Price "that MGDG synthase is 24% identical to YpfP is significant but not sufficiently so to indicate that both proteins have the same function." Page 4961, left-hand column, last paragraph. Further, there is

no conclusion of the authors or any other hint into the direction of the finding of the present invention, that is, the novel function of processive lipid glycosyl transferase.

Also, there is no motivation to combine the references. With respect to Sorokin and Kunst, the Examiner admits that both references fail to teach that the polypeptide is a processive glycosyl transferase which is able to transfer sugar molecules to lipid substrates in order to synthesize glycolipids. This "gap" in the prior art of Sorokin and Kunst is simply filled by the Examiner with the benefit of hindsight by combining the sequences of Sorokin and Kunst with the non-processive enzyme teaching of Price. However, as discussed above, Price explicitly states that the similarity between MGDG synthase and YpfP is not sufficient to indicate that both proteins have the same function. Further, it is by no means obvious to one of ordinary skill in the art to take the sequences provided by Kunst or Sorokin and use them in a process as claimed in the present application. Applicants strongly disagree that one of ordinary skill in the art would conclude that the enzyme has processive activity after analyzing the glycolipids formed. Also, the Examiner seems to ignore that even the combined view of Sorokin/Kunst and Price do not teach the use of a processive lipid glycosyl transferase in the production of glycolipids in transgenic cells or organisms. Therefore, the combination of these references is artificial and is clearly based on hindsight.

For all of the above reasons, Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 103, and allowance of the pending application.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the specification and the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 11/6/02

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Please amend Claims 1-5 as follows:

1. (Twice Amended) A process for the production of glycolipids in transgenic cells and/or organisms **using a processive lipid glycosyl transferase that successively transfers hexose residues to a lipid acceptor**, comprising:

- transferring a nucleic acid molecule that codes for a protein having the **[biological]enzymatic** activity of a processive diacylglycerol glycosyltransferase to the cells or organisms,

- expressing the protein having **[a biological]the enzymatic** activity of a processive diacylglycerol glycosyltransferase under suitable regulatory sequences in the cells or the organisms, and

- recovering glycolipids synthesized by the **[biological]enzymatic** activity of a processive diacylglycerol **[glycosykltransferase]glycosyltransferase** from the cells or the organisms **if desired**.

2. (Twice Amended) The process according to claim 1, wherein the nucleic acid molecule codes for a protein having the **[biological]enzymatic** activity of a processive **[diacylglycerol]lipid** glycosyl transferase from *Bacillus subtillus* or *Staphylococcus aureus*.

3. (Twice Amended) The process according to claim 1, wherein the transgenic cells are selected from the group consisting of plant, yeast and **[bacteria]bacterial** cells, and the organism is a plant.

4. (Twice Amended) The process according to Claim 1, wherein the glycolipids are **selected from the group consisting of** glycosyl diacylglycerols, **sterolglycosides, glycocerebrosides,[and/or]** phosphoglycolipids, **and any combination thereof**.

5. (Twice Amended) The **process** according to Claim 1, wherein the glycolipids are selected from the group consisting of

- monoglycosyldiacylglycerol,

- diglycosyldiacylglycerol,

- triglycosyl diacylglycerol,
- tetraglycosyldiacylglycerol,
- glycosyl ceramide,
- diglycosyl ceramide,
- steryl glycoside,
- steryl diglycoside,
- glycosyl phosphatidylglycerol, and
- diglycosyl phosphatidylglycerol.